

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- ✓ TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS.

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

What is claimed is:

- 1 1. A substantially pure polypeptide complex comprising a Clostridium
2 botulinum neurotoxin and more than one Clostridium botulinum type E neurotoxin
3 associated polypeptide.
- 1 2. A complex of claim 1, wherein the neurotoxin associated polypeptide has a
2 molecular weight of approximately 80 kDa and comprises the amino acid sequence
3 TNLKPYYIYD (SEQ ID NO:4).
- 1 3. A complex of claim 1, wherein the neurotoxin associated polypeptide has a
2 molecular weight of approximately 65 kDa and comprises the amino acid sequence
3 MQTTTLNWDY (SEQ ID NO:3).
- 1 4. A complex of claim 1, wherein the neurotoxin associated polypeptide has a
2 molecular weight of approximately 40 kDa and comprises the amino acid sequence
3 MRINTNINSM (SEQ ID NO:2).
- 1 5. A complex of claim 1, wherein the neurotoxin associated polypeptide has a
2 molecular weight of approximately 18 kDa and comprises the amino acid sequence
3 MKQAFVFEFD (SEQ ID NO:1).
- 1 6. A complex of claim 1, wherein the neurotoxin associated polypeptide has a
2 molecular weight of approximately 18 kDa and comprises the amino acid sequence shown in
3 Fig. 8 (SEQ ID NO:5).
- 1 7. A substantially pure Clostridium botulinum serotype E neurotoxin associated
2 polypeptide.
- 1 8. The polypeptide of claim 7, wherein the neurotoxin associated polypeptide
2 has a molecular weight of about 80 kDa.

1 9. The polypeptide of claim 8, wherein the neurotoxin associated polypeptide
2 comprises the amino acid sequence TNLKPYYIYD (SEQ ID NO:4).

1 10. The polypeptide of claim 7, wherein the neurotoxin associated polypeptide
2 has a molecular weight of about 65 kDa.

1 11. The polypeptide of claim 10, wherein the neurotoxin associated polypeptide
2 comprises the amino acid sequence MQTTTLNWDY (SEQ ID NO:3).

1 12. The polypeptide of claim 7, wherein the neurotoxin associated polypeptide
2 has a molecular weight of about 40 kDa.

1 13. The polypeptide of claim 12, wherein the neurotoxin associated polypeptide
2 comprises the amino acid sequence MRINTNINSM (SEQ ID NO:2).

1 14. The polypeptide of claim 7, wherein the neurotoxin associated polypeptide
2 has a molecular weight of about 18 kDa.

1 15. The polypeptide of claim 14, wherein the neurotoxin associated polypeptide
2 comprises the amino acid sequence MKQAFVFEFD (SEQ ID NO:1).

1 16. The polypeptide of claim 14, wherein the neurotoxin associated polypeptide
2 comprises the amino acid sequence shown in Fig. 8 (SEQ ID NO:5).

1 17. A substantially pure antibody that specifically binds to a Clostridium
2 botulinum type E neurotoxin associated polypeptide having a molecular weight of
3 approximately 80, 60, 45, or 18 kDa, or to a complex of any two or more of said neurotoxin
4 associated polypeptides.

1 18. A substantially pure antibody that specifically binds to a polypeptide complex
2 of claim 1.

1 19. A method of detecting a serotype E neurotoxin complex in a sample, the
2 method comprising:

- 3 (a) contacting the sample with an antibody of claim 17, and
4 (b) detecting antibody-bound polypeptide, if any, in the sample, the presence of
5 antibody-bound polypeptide indicating the presence of serotype E neurotoxin in the sample.

1 20. The method of claim 19, wherein the sample is a foodstuff.

1 21. The method of claim 19, wherein the sample is a gastrointestinal, blood, or
2 tissue sample obtained from a vertebrate animal.

1 22. A method of treating a patient who is suffering from a disease or condition
2 associated with excessive release of acetylcholine from presynaptic nerve terminals, the
3 method comprising administering to the patient a therapeutically effective amount of a
4 polypeptide complex of claim 1.

1 23. The method of claim 22, wherein the excessive acetylcholine release causes
2 undesirable contraction of smooth or skeletal muscle cells.

1 24. The method of claim 22, wherein the excessive release of acetylcholine causes
2 profuse sweating, lacrimation, or mucous secretion.

1 25. A method of treating a patient who is suffering from spasticity occurring
2 secondary to brain ischemia, or traumatic injury of the brain or spinal cord, the method
3 comprising administering to the patient a therapeutically effective amount of a polypeptide
4 complex of claim 1.

1 26. A method of treating a patient who is suffering from tension headache or pain,
2 the method comprising administering to the patient a therapeutically effective amount of a
3 polypeptide complex of claim 1.

1 27. A vaccine comprising a polypeptide complex of claim 1.

1 28. A method of vaccinating an animal against serotype E neurotoxin, the method
2 comprising administering to the animal an effective amount of the vaccine of claim 27.

1 29. A vaccine comprising a polypeptide of claim 7.

1 30. A method of detecting a Clostridium botulinum serotype E neurotoxin in a
2 sample, the method comprising:

3 (a) contacting the sample with a Clostridium botulinum type E neurotoxin associated
4 polypeptide (NAP) of claim 7 that specifically binds a serotype E botulinum neurotoxin and
5 thereby forms a NAP-neurotoxin complex, and

6 (b) detecting the NAP-neurotoxin complex, if any, in the sample, the presence of a
7 complex indicating the presence of serotype E neurotoxin in the sample.

1 31. A complex of claim 1, comprising the neurotoxin and neurotoxin associated
2 polypeptides having molecular weights of about 80 kDa, 65 kDa, 40 kDa, and 18 kDa.

1 32. The complex of claim 1, comprising the neurotoxin and neurotoxin associated
2 polypeptides having molecular weights of about 118 kDa, 80 kDa, 65 kDa, 40 kDa, and 18
3 kDa.